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# Clinical Proceedings

## OF THE CHILDREN'S HOSPITAL

## WASHINGTON, D. C.

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# to help you combat iron deficiency in infants...

**How Fer-In-Sol improved infants' blood pictures**

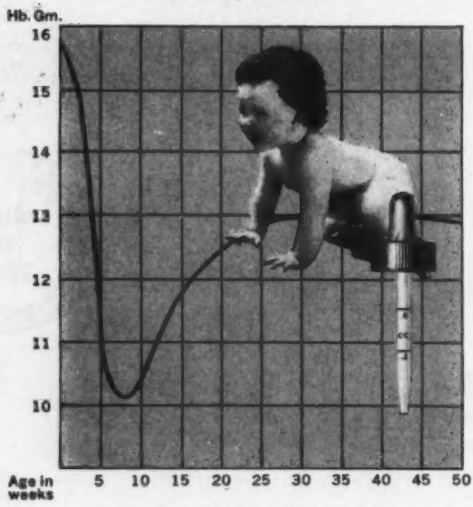


Chart adapted from Niccum, Jackson and Stearns: A.M.A. Am. J. Dis. Child. 86: 553, 1954.

Mean hemoglobin determinations of infants on a predominantly milk diet receiving Fer-In-Sol. The Fer-In-Sol dose was 5 mg. of iron (0.2 cc.) per day at 3 months, increased to 10 mg. of iron (0.4 cc.) after 6 months of age.[1]

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(1) Niccum, W. L.; Jackson, R. L., and Stearns, G.: A.M.A. Am. J. Dis. Child. 86: 553, 1954. (2) Smith, C. H.: Bull. New York Acad. Med. 30: 155, 1954. (3) Smith, N. J., and Rosello, S.: J. Clin. Nutrition 1: 276, 1953. (4) Sturgeon, P.: Pediatrics 13: 107, 1954.

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# ABDOMINAL PAIN IN INFANTS AND CHILDREN

Preston A. McLendon, M.D.*

Joseph M. LoPresti, M.D.**

Abdominal pain occurs as a part of the symptom complex of numerous diseases in infants and children. In many instances the pain accompanies a relatively inocuous disease, such as food indiscretion. On the other hand, it may indicate the need for surgical exploration of the abdomen. This differentiation may not be easy particularly when the abdominal pain is vague, nonspecific and recurrent. Occasionally it may be obvious that the pain is psychologic in origin; in other cases, organic or physiologic causes may form the basis for this complaint; and in still others, all these factors may be present. Many times the problem can be resolved only by resorting to laboratory procedures. In the child with recurrent abdominal pain associated with pyuria, an intravenous pyelogram may be indicated. When other gastrointestinal symptoms are present, x-ray studies may be needed. The accompanying symptomatology, the course of the illness, and the positive physical findings will indicate the need for further investigation and the direction which these studies should follow.

Abdominal pain is manifested in infants by screaming or constant crying, restlessness, irritability, squirming, grunting respirations, flexion of the thighs on the abdomen, and refusal to eat.

"Colic" is a relatively common, nonspecific symptom state occurring in the first few months of life. It is characterized by vigorous and prolonged crying presumably due to intermittent abdominal pain. Crying may not diminish even though the baby is picked up. The incidence and frequency of colic varies in different social groups and families. In some it occurs only occasionally and is seen infrequently; in others, this disturbance is experienced almost every evening for two or three months. This common syndrome may be due to many factors. Errors in feeding technique are important: excessive air swallowing; improperly sized nipple holes; bottle propping; and the ingestion of an improper quantity and quality of formula. Underfeeding as well as over feeding should be investigated. At times gastrointestinal allergy may play a role. Allergy to cow's milk is a common cause of "colic", especially when visible gastric peristaltic waves and the passage of loose stools which contain mucus and occasionally blood, are present. In some infants "colic" may reflect tenseness in the mother and household. It is advisable to examine carefully all babies whose mothers report unexplained crying.

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To establish the exact cause of abdominal pain in the younger age group, a careful, searching history of the present illness and feeding habits is essential. Most important are the positive physical findings. Auscultation of the abdomen appears to have become a lost art in medicine. Valuable information may be derived from this relatively simple procedure. The "silent" abdomen with short, high pitched peristaltic waves is almost pathognomonic of complete intestinal obstruction whether organic or adynamic while hyperperistalsis is usually present in specific or nonspecific enteritis. Perhaps the most important information is derived from palpation of the abdomen. It will elicit normal and abnormal tension of the abdomen and its contents, the state of tissue turgor and hydration, and the presence or absence of tenderness and rigidity. Normal and abnormal organs and masses may be outlined and evaluated.

In infants and children the technique of palpation differs from that employed in examining the adult. It should be as gentle as possible because more information can be derived in this way. In addition, a gentle touch will spare the child unnecessary pain and the likelihood of inviting resistance will be lessened. The approach to any tender area should always be from a little distance and should always be gradual in order to assure the child that he will not be hurt suddenly or unnecessarily. The warm hand is laid flat on the abdomen and light palpation made with the ends of the fingers. Deep, prolonged, and repeated palpation, especially by several examiners, should be avoided to spare the child needless discomfort and to guard against the danger of trauma. In eliciting tenderness it is almost valueless and even may be misleading to ask repeatedly whether "this spot" or "that spot" is tender or "hurts". This is true even in the older child. More reliable information may be gained by watching the child's face. Even the slightest tenderness is reflected by an involuntary facial expression of pain. If the pain is more severe local resistance will be encountered, the child will make an attempt to get away from the examiner's hand, or there will be an unmistakeable "ouch", or even tears. The younger the child the more dependable this reaction. Only in the older child does one occasionally find inconstant and shifting tenderness. Voluntary rigidity has the same significance as tenderness. It is a voluntary protection against pain and is variable. Involuntary rigidity is automatic. It is immediate, constant and boardlike and means peritoneal inflammation whether local or generalized. In the infant and younger child and even in the older "nervous" child, it is often necessary to be most patient and tactful. One can often determine that apparent rigidity is not actual rigidity by keeping the hand resting gently on the abdomen while giving the baby a bottle or letting him nurse or while distracting an older child. Involuntary rigidity along with tenderness has more significance than tenderness alone.

Pain and tenderness usually go together but they are by no means of equal degree in various conditions. *Pain* is more severe than *tenderness* in all "colics" regardless of their causes. An important differential point is the fact that pressure is commonly applied to lessen the pain of colic, whereas it is avoided if there is marked tenderness caused by inflammation or any other factor. In referred pains such as those which are encountered in pneumonia and pericarditis, pain is more severe than tenderness. Right lower lobe pneumonia with diaphragmatic pleurisy, in particular, may cause abdominal pain, vomiting and, at times, muscle guarding on the right. These symptoms may strongly suggest acute appendicitis. Tenderness is more marked than pain in acute appendicitis. The exception to this occurs when the inflamed appendix is located retrocecally. In these patients there is little tenderness while pain is a constant feature.

Appendicitis is the commonest cause for abdominal surgery in childhood. While the diagnosis is usually obvious, at times it may present one of the more difficult diagnostic problems. This is especially true in infants and young children. Classically appendiceal inflammation begins with abdominal pain followed by nausea and vomiting and finally by the appearance of fever. Frequently the pain is localized at first in the periumbilical or epigastric regions. After a period of time, pain shifts to the lower right quadrant. It usually is constant and not too severe, but it may be "colicky" or intermittent. Vomiting is almost a constant feature of appendicitis in childhood. It may occur once, twice or repeatedly, though violent vomiting and "retching" are infrequent. Unless a complication occurs, fever usually is low grade. In infants symptoms associated with this condition may be overlooked. These include unusual irritability, restlessness, unexplained crying, and refusal of feedings. Typically, if rupture of the appendix occurs the child may become almost symptom-free for a few hours. The pain soon returns, however, with increased intensity. If the classical findings of appendicitis have not developed when the patient is first seen, close observation is indicated with repeated examinations over a period of a few hours. Usually it is best to hospitalize these patients unless close personal supervision can be provided in the home. Attention has been drawn repeatedly to the frequency with which acute appendicitis occurs as a complication of measles. It may also occur in children who have an upper respiratory infection, enteritis, rheumatic fever or other diseases which in themselves may be characterized by abdominal pain.

Acute mesenteric adenitis is the condition which simulates appendicitis most closely. Many times the differentiation is impossible except by operation. This acute inflammatory process involving the mesenteric lymph nodes is usually associated with tonsillitis and pharyngitis. The presenting symptom is abdominal pain, which may be generalized or localized any-

where in the abdomen. Many times nausea is present and vomiting may occur. Fever of varying degree is present and there may be an accompanying leukocytosis. The condition is usually benign and the symptoms subside as the throat infection clears up.

In infants with abdominal pain, intussusception is an important consideration. Early diagnosis and treatment are imperative if mortality is to be reduced. It is characterized by the sudden onset of extreme pain which, after a variable period of time disappears almost as suddenly, only to be followed by a similar episode. This sudden onset is extremely valuable. In almost no other condition can the mother state the exact hour at which the abdominal pain began. In the course of some hours the pains become less severe. The facies usually becomes so distinctive that, this, too, is of diagnostic value. The infant appears calm, paying little attention to his surroundings and yet seems preoccupied and apprehensive. Vomiting may occur early, but, like blood in the stools, usually is a late manifestation. At times a barium enema may be necessary to establish the diagnosis.

Chronic or recurrent abdominal pain always should direct the physician's attention to the urinary tract. The most important type of urinary tract disease associated with this symptom is an obstruction with or without superimposed infection. Fever, nausea or vomiting may or may not be present. Repeated bouts of pyuria are an indication for a complete investigation of the urinary tract. Abdominal pain occurs occasionally as an early manifestation of acute glomerulonephritis.

In approximately one-third of the children with acute rheumatic fever, pain in the abdomen is an early manifestation. Frequently it will precede the appearance of other major and minor signs. Usually the abdominal pain is diffuse or present in the epigastric area; abdominal tenderness and rigidity may not be present. This symptom may be accompanied by fever, vomiting and leukocytosis. Occasionally localizing findings may occur in the right lower quadrant. In such children, the differentiation between the abdominal manifestations of rheumatic fever and appendicitis may be difficult or impossible. Sometimes it will be of diagnostic value to give a trial of salicylates from which a dramatic response may be obtained if the symptom is a manifestation of acute rheumatic fever.

In recent years it has been demonstrated that paroxysmal episodes of abdominal pain may be associated with abnormal cerebral discharges. This symptom is a common aura of epileptic convulsions. Nausea and vomiting may or may not occur during these episodes. The abdominal pain is acute, severe and "colicky", and periumbilical or epigastric in origin. It may last from a few minutes to hours and may be followed by a period of somnolence. Episodes of abdominal pain may recur several times over a period of a few days. The electroencephalographic tracing is often abnormal. These patients may or may not have a history of generalized convulsions.

Since pain ("it hurts") is one of the early patterns which children learn, it is natural for an older child to use this expression for psychological reasons. Since pain is a subjective complaint it is difficult at times to disprove its presence. Adults frequently refer to their abdominal discomforts in the presence of children. It becomes then, very simple for the child to use the abdomen as a site for psychological reference. This may be the result of pressure about eating habits or the distress experienced in other situations about the house or at school. Many of the distressing school situations produce "pain" in the abdomen on getting up in the morning. When related to mealtime pressures, it occurs just before or during the meal. In these instances a most careful and searching history of home and school attitudes will reveal a clear-cut psychogenic reason. Some children carry this complaint to such a point that laboratory help is needed. Tenderness may be complained of on palpation but no muscle rigidity (especially spasm), can be elicited. A psychogenic basis for abdominal pain should be concluded only after organic disease has been eliminated.

Detailed description of the many specific diseases causing abdominal pain is not feasible here. There is appended a list of such causes. In many children the diagnosis will be apparent merely from an evaluation of the history of the present illness and the physical findings. In others laboratory procedures such as x-rays of the chest or abdomen, hematologic studies, examination of the stools and urinanalysis will aid in establishing exact etiology. In a few instances more elaborate diagnostic procedures such as barium studies of the gastrointestinal tract, pyelography, electrocardiography, and electroencephalography will be needed before the diagnosis can be pinpointed. There is no substitute for a careful, painstaking, and searching history of the illness together with a gentle, patient and thorough physical examination for the evaluation of abdominal pain. The findings will indicate to the physician which of the laboratory studies, if any, is indicated. Experience and practice often will spare the patient much needless expense, the trauma of hospitalization, and unnecessary surgery.

### Common Causes of Abdominal Pain in Infants and Children

I. Psychological

II. Extra-Abdominal

- A. Lungs, e.g., pneumonia
- B. Heart, e.g., rheumatic fever, pericarditis
- C. Central nervous system, e.g., abdominal epilepsy, tumors.
- D. Blood dyscrasias, e.g., hemolytic anemias, sickle cell anemia, anaphylactoid purpura, leukemia.
- E. Metabolic, e.g., diabetic acidosis, hypoglycemia, lead intoxication.

III. Intra-abdominal

A. Gastro-intestinal tract, e.g., "colic", food indiscretion, appendicitis, intussusception, volvulus, mesenteric adenitis, enteritis, incarcerated hernia, allergy.
B. Genito-urinary tract, e.g., anomalies, infection, calculi, glomerulonephritis.
C. Liver and spleen, e.g., trauma, infectious hepatitis, congestion.
D. Ovaries, e.g., torsion of ovarian cyst, Mittleschmerz syndrome.
E. Miscellaneous, e.g., peritonitis, iliac adenitis.

## RHEUMATIC FEVER WITH HEART DISEASE

### Sunday Morning Conference

Bernard J. Walsh, M.D.*

John O. Nestor, M.D.**

In these years, in the last 15 years particularly, and continuing up to the present, as the incidence of rheumatic fever and therefore rheumatic heart disease falls in the civilized world, it probably will become increasingly important to have an occasional session like this because of the infrequency with which the physician will see rheumatic fever.

#### CASE I

This 7 year old colored boy was admitted to this hospital on September 10, 1955, after two days of lethargy, hyperpnea, cough, and palpitation. At the onset of his symptoms he was seen in the Out Patient Department where examination revealed pulse 108, respirations 48, clear lungs, cardiomegaly with the point of maximum impulse in the sixth left intercostal space outside the nipple line, and Grade IV apical systolic murmur transmitted to the left axilla and right scapula. The liver was palpable 1 cm. below the right costal margin but examination was otherwise normal. The child was referred to cardiology clinic where he was seen on the day of admission. At this time his pulse was 120, his liver was not enlarged, and examination of the heart revealed a double thrill and murmur at the apex, an accentuated and split $P_2$, and fairly marked cardiomegaly.

Past history revealed that on routine examination 1½ years previously, a murmur was heard. The patient was studied at another hospital where a diagnosis of possible rheumatic heart disease was made after electrocardiogram, x-ray of the chest and physical examination. He was referred to this hospital for further evaluation. There was no history of an illness which could have been construed as active rheumatic fever.

At his first visit to our cardiac clinic on May 20, 1954, examination showed a

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slightly harsh, long systolic murmur heard best at the apex and transmitted to the sternum and axilla. Fluoroscopy showed minimal enlargement of the left ventricle, and electrocardiogram was within normal limits. Sedimentation rate was 13 mm per hour and blood studies were normal. It was felt that the patient had inactive rheumatic heart disease with mitral regurgitation, and he was placed on prophylactic sulfisoxazole therapy. He was seen at intervals of two to six months in the cardiology clinic and on each occasion the same physical findings were noted until the present illness began.

On admission and throughout his course, urinalysis was normal. Blood count on admission revealed a mild anemia and relative polymorphonuclear cell predominance with normal total leukocyte count. The anemia persisted but the leukocyte count fluctuated between 5,700 and 14,200. Initial sedimentation rate was 22 mm per hour, anti-streptolysin "O" titer 100 units per ml, and C-reactive protein negative. Although the anti-streptolysin "O" titer and C-reactive protein never became elevated, the sedimentation rate fluctuated between 11 mm per hour and 18 mm per hour.

Electrocardiogram on admission showed a PR interval of 0.18 second, interpreted as first degree atrio-ventricular block. This finding persisted on each electrocardiogram except on November 17 when frequent premature ventricular contractions were noted along with evidence of abnormal myocardium.

In the hospital initial therapy consisted of bed rest, regular diet, and intramuscular procaine penicillin, 400,000 units daily. On September 12, 1955 prednisone therapy was begun with maintenance at 10 mg. four times a day. On September 23, 1955, intramuscular penicillin was replaced by 200,000 units of oral penicillin every 8 hours. On September 27, 1955 there was no evidence of improvement; pulse was still 120, murmurs and cardiomegaly were the same and he had some "moon face". Venous pressure on September 28 was 190 mm of saline. By October 13, 1955 there was still no improvement, and hepatomegaly and pulmonary edema were noted. He was given thiomerin 0.5 cc intramuscularly and started on theocalcin 1.0 gm three times daily for two weeks with some decrease in pulmonary edema and hepatomegaly. On October 25, 1955 gradual reduction in prednisone dosage was begun.

Fever ranging from 100° to 102° developed on November 3 and continued for 2 weeks during which time there were several episodes of vomiting with occasional bright hematemesis. There also developed hepatomegaly, pulmonary edema, cough and bright hematemesis. During this time the patient received oxygen by tent as needed, a low salt, bland diet, chlorpromazine and chloramphenicol. He was given two packed red blood cell transfusions, and because of increasing cardiac decompensation received 1.0 cc of thiomerin intramuscularly on November 15, 1955 with slight improvement. On November 16, 1955 theocalcin was again begun at dosage of 0.5 gm three times daily. Oral digitalization with digalen was begun. The digitalizing dose was 720 mg given in 3 doses, and maintenance was then begun with 77 mg daily. Because of electrocardiographic evidence of digitalis toxicity, digalen was stopped on November 18, 1955. The digalen dose was adjusted to a final maintenance at 33 mg orally daily beginning on November 24, 1955. At this point the patient had no pulmonary edema or hepatomegaly; his pulse was 80 and regular; his heart was still markedly enlarged, and murmurs showed no significant change. His condition remained static, and he was transferred to a convalescent home on December 20, 1955, still on maintenance digalen therapy.

### CASE II

This 10 year old colored boy was admitted to this hospital for the second time on August 4, 1955 because of dyspnea, cardiomegaly, and a murmur typical of mitral

regurgitation. Review of his history indicated that he had become ill about March 10, 1955 with fever, malaise, pain and swelling of the joints, tachycardia, and systolic murmur. A few days previously he had recovered from a sore throat.

On March 20, 1955 he was admitted to a hospital in North Carolina where therapy was begun with aspirin and hydrocortisone. Five days later he was admitted to this hospital where initial physical examination revealed temperature of 99.6°F, pulse 90, and the point of maximum cardiac impulse in the sixth left intercostal space at the anterior axillary line. The left heart border was enlarged on percussion. There was a Grade I or II blowing, apical murmur, filling most of systole and radiating to the second left intercostal space parasternally. The liver edge was felt 2 cm below the right costal margin. There was bilateral ankle and pedal edema, and the elbow, ankle and knee joints were slightly swollen, warm and tender. Laboratory studies then showed rapid sedimentation rate, elevated antistreptolysin "O" titer and leukocytosis. X-ray showed an enlarged left cardiac border, and electrocardiogram was within normal limits. Therapy was begun with aspirin and prophylactic penicillin.

During a 3 week stay in this hospital, his heart size decreased somewhat; his murmur reduced to Grade I and remained localized to the apical area; and his joints became normal. Midway in his course, tonsillitis developed but subsided with penicillin and sulfonamide therapy. On March 18, 1955 he was transferred to the convalescent unit at D. C. General Hospital for 2½ months. Two weeks prior to his second admission the patient spent 2 weeks at a camp for cardiacs where again joint pain and swelling developed.

On his second admission (August 4, 1955) examination revealed a temperature of 100.5°F, pulse 115, dyspnea, and general malaise with swelling and limitation but no tenderness or heat in the ankle and knee joints. The heart was enlarged with the point of maximum impulse in the seventh left intercostal space at the anterior axillary line. A harsh apical systolic murmur radiated to the axillae. Fluoroscopy showed enlargement of the left auricle and both ventricles. Electrocardiogram showed only left ventricular preponderance. Blood studies showed a normal leukocyte count and differential with antistreptolysin "O" titer of 2,500 units, sedimentation rate of 45 mm per hour, and C-reactive protein 2 plus. Venous pressure was 138 mm of water. Therapy consisted of prophylactic penicillin, prednisone in dosage of 10 mg every 6 hours, as well as low salt diet and bed rest. Within one week of admission he was afebrile and asymptomatic. His extremities were normal but his heart showed no change. On August 22, 1955 he spiked fever to 102° with a follicular tonsillitis due to *Staphylococcus aureus*. This responded after one week of oxytetracycline and penicillin therapy. He again remained afebrile and asymptomatic. By September 7, 1955 his C-reactive protein was negative, antistreptolysin "O" titer was 166 units, leukocyte count and differential normal, but the sedimentation rate was still 45 mm per hour. On September 12, 1955 he was transferred to the D. C. General Hospital convalescent unit for further care. He was seen in our cardiac clinic for follow up in December 1955, January and February 1956, and on each occasion examination revealed no change in physical findings.

## DISCUSSION

### John O. Nestor, M.D.

The first case was seen in our Cardiac Clinic six months before his present hospitalization for the evaluation of a heart murmur detected by his school physician. Although there was no history suggesting that he had had an attack of acute rheumatic fever, nevertheless, he had the classical murmur

of mitral insufficiency with slight cardiac enlargement and was labelled as having inactive rheumatic heart disease with mitral insufficiency and placed on daily doses of sulfisoxazole as prophylaxis against respiratory infection.

Despite the prophylaxis severe active rheumatic carditis occurred as the only major manifestation of rheumatic activity and the boy was admitted to the hospital without fever and with the usual laboratory procedures yielding values within normal limits or borderline. The only exception was the electrocardiogram which revealed first degree atrioventricular block.

The second case was correctly diagnosed as having active rheumatic fever and polyarthritis in North Carolina where he received antibiotics, salicylates, and hormonal therapy although there was no evidence of clinically significant heart disease in the form of cardiac enlargement or a classical murmur. He was transferred to Children's Hospital where the diagnosis of active rheumatic fever without carditis was confirmed. He had a slight soft musical systolic murmur along the left sternal border which was obviously functional and his heart was within normal limits on x-ray. After three weeks he was transferred to the Rheumatic Fever Unit at D. C. General Hospital where during his entire stay of two and one half months he showed no evidence of having rheumatic heart disease. He was then permitted to attend the cardiac camp and at the precamp physical examination he had no evidence of heart disease and was placed on sulfisoxazole prophylaxis. Three weeks later on returning from camp he was admitted here with definite evidence of active rheumatic heart disease with mitral insufficiency and enlargement.

Bernard J. Walsh, M.D.

These patients presented here are interesting because they are actually in some contrast to one another. They illustrate possible courses of the disease; actually illustrate what are not by any means rare characteristics. Particularly the disease in the first boy demonstrates some unusual features but again I should emphasize that they are not rare. This boy of course had severe rheumatic fever. He had it without fever and without a fast sedimentation rate even before he had any congestive failure. He had a negative C-reactive protein and an antistreptolysin "O" titer was not outside the range of normal. As this first boy illustrates perfectly well, if you wait to make a diagnosis of rheumatic heart disease for a history of clear cut rheumatic fever in an individual with a murmur of mitral regurgitation, of course you are not going to make the diagnosis. Correct diagnosis is going to be omitted in certainly 5 to 10 per cent of children who have rheumatic heart disease under these circumstances. There is nothing unusual at all about seeing a child, such as you saw in this first case, who was sent in for evaluation of a heart murmur, who has lived only six to eight years and whose

parents believe that he has had no illness that you could consider to be rheumatic fever and yet he has rheumatic heart disease. The significance of that diagnosis I think is borne out here, unfortunately for this boy, because rheumatic fever has recurred with evident progressive heart disease, indicating of course that the original diagnosis was correct. In other words, if a patient has a slight, moderately loud, long harsh systolic murmur maximum at the cardiac apex, if you can exclude significant anemia, bacterial endocarditis, any type of congenital heart disease with mitral regurgitation, all of that being as a rule, pretty easy, then the diagnosis is rheumatic heart disease with mitral regurgitation, no matter what the size of the heart, no matter what the history. We, of course, labeled him last year as having rheumatic heart disease with mitral regurgitation though he had no history as to when his rheumatic fever occurred. We put him, as we put them all, (and have for 14 or 15 years at least) on regular prophylactic doses of either sulfonamides, or in the last two or three years on regular doses of oral penicillin. In the recent meeting in New Orleans, Dr. Gil Blount of Denver, in commenting on the prophylactic medication that is given to these people or is recommended for them, described a short study to determine how many of them took it. Even though they had it in their possession, only 23 per cent of his group actually took the sulfonamide or penicillin regularly every day. This was emphasized in another way by a member of another panel on the prophylactic therapy of rheumatic fever, having to do with the clinic patients in Children's Memorial Hospital in Chicago. Dr. Seigel commented that these patients were having recurrences, even though they had the prophylactic drugs, and were told how to take it, and the importance of taking them was emphasized to them and to their parents. When they had the child coming in every month, which is really not necessary otherwise, and sent the nurse to the home, they found that the incidence of streptococcal infection, streptococcal pharyngitis, and recurrent rheumatic fever in the group who had had rheumatic fever previously, and who had had the sulfonamide or the penicillin, fell very greatly. It does not do them any good if they have it and they do not take it. In fact it is highly probable that this boy would not be where he is if he had taken sulfonamide regularly, because sulfisoxazole and other sulfonamides work about as well prophylactically as does penicillin. Despite the fact that he had an antistreptolysin titer within normal limits, I have little doubt but that he had a group A hemolytic streptococcal infection to precipitate his rheumatic fever.

A comment about abdominal pain may be worthwhile because those dealing with children of course, soon learn that abdominal pain, nonspecific and generalized, and sometimes quite severe, is one of the first symptoms of rheumatic fever. In our experience, abdominal pain is seen in between 15 and 20 per cent of patients with active rheumatic fever and in

another 4 or 5 per cent it appears later. The reason for it, the origin of it, the cause of it in rheumatic fever patients has never been determined and perhaps never will be. The fact that it does occur and may be the first symptom, the reason for which the doctor is called, the reason the child is brought to the hospital, means that it cannot be overemphasized when one considers also the possible surgical implications.

I think it is evident to everyone why we know this boy has rheumatic fever at this time. This boy had had progressive cardiac enlargement since we saw him in January. He previously had the murmur of mitral regurgitation with the heart size as you saw it and on the very day he came in here he had a loud diastolic murmur at his cardiac apex which he had not had in January. That murmur is louder now; his heart is hyperactive as you saw; his heart has increased in size. There is no other explanation for that unless you postulate that he has bacterial endocarditis or a serious and severe protracted anemia such as might occur with leukemia. As far as therapy is concerned, here is a child in whom congestive heart failure developed while he was taking prednisone. The real value of ACTH and cortisone in treatment of rheumatic fever has not been settled and at the moment it looks as if it never will be. Probably, as a routine, these drugs do not have any more value than aspirin. In occasional patients I think all of us feel that we have done some good for a patient with ACTH or steroids; that we have helped to a degree that we would not expect with aspirin. There is no proof up to this very minute that cortisone or ACTH are better than aspirin in the therapy of rheumatic fever. The cooperative clinical studies sponsored by the American Heart Association were reported early in the year in "Circulation" on a basis of 750 patients treated in 8 different centers, 5 in this country, 1 in Canada, and 2 in England. These patients were treated as objectively as was humanly possible to do and there was not the slightest bit of evidence that cortisone or ACTH were in any way superior to aspirin in the treatment of those patients with rheumatic fever. These findings are borne out in the first case because this boy's rheumatic carditis grew worse after he had been receiving prednisone for more than two weeks. One could argue at this point, I suppose that perhaps he was not in congestive heart failure; perhaps it was due to sodium retention, but I do not think so. There was little evidence of hypercorticism at the time his liver was large, aside from some mooning of his face; he never had any significant hypertension; he had no acne or striae; and he certainly responded very nicely to mercurial diuretic and theocalcin so far as his heart failure was concerned.

As to the second boy, he is doing well again. He is at our rheumatic fever convalescent center from which he left to go to camp as Dr. Nestor has indicated. Unfortunately, through some administrative error he did not take regular prophylactic penicillin while at camp. That is probably the

problem here so far as his recurrence is concerned. Of course the actual features of his recurrence are the standard ones. He has a very high antistreptolysin titer indicating that he had a beta-hemolytic streptococcal infection sometime recently and you can see that the fact that it fell very nicely to 166 units before he left the hospital, was highly suggestive that it was a recent infection. The fact that this infection reprecipitated rheumatic fever which in turn produced rheumatic heart disease that he did not previously have, if nothing else, re-emphasizes the importance of taking prophylactic antibiotics or sulfa. As of today, we are using ordinary potassium penicillin, 250,000 units once a day before breakfast. There is every reason to believe that, with few exceptions, this will prevent streptococcal infection and thereby prevent actual return of rheumatic fever. There is mounting evidence and I think, for practical purposes, conclusive evidence that the long time suspicion that beta-hemolytic streptococcal infection was intimately related to rheumatic fever is true. Therefore, if you can prevent the infection you can prevent the recurrence.

## CLINICAL PATHOLOGICAL CONFERENCE

Discussed by: Roland B. Scott, M.D.,* Neville K. Connolly, M.D.,** F. R. Leyva, M.D.**

Directed by: E. Clarence Rice, M.D.

Assisted by: Grace Guin, M.D., Enid Gilbert, M.D.

### CLINICAL SUMMARY

Enid F. Gilbert, M.D.

This 6 year old white boy was admitted to Children's Hospital deeply cyanotic and in a moribund condition. He died two hours following admission.

The past history revealed that ten days after birth he became deeply jaundiced. This persisted until the age of 2 months, during which time his stools were pale and his urine very dark. His subsequent development was normal, but his parents occasionally noted a light yellow tint of the eyes. This icterus was not related to infections or any other factor that the parents could recall. He was seen by a pediatrician frequently during the first 6 months of life, and his growth and nutrition were normal. During

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the first four years of his life, his parents were aware of a moderate enlargement of his abdomen, but attached no significance to this. During the fourth year of life the patient had acute follicular tonsillitis and for the first time since infancy was taken to a physician. The examination by the physician disclosed marked enlargement of both liver and spleen, and the patient was referred to Children's Hospital for medical observation and diagnosis.

Physical examination at this time revealed a well developed, well nourished, white male child with a markedly protuberant abdomen and icteric sclerae. His tonsils were acutely inflamed and there was some folliculitis. The heart and lungs were normal. Examination of the enlarged abdomen revealed a small umbilical hernia, and a pattern of small, distended superficial veins over the anterior surface of the abdomen. The liver extended midway between the right costal margin and the umbilicus. It was firm, non-tender, and both large and small nodules were palpated along the edge. The spleen extended to the umbilical line and was markedly firm and non-tender. No other organs, masses, or free fluid were noted in the abdomen.

The family history was non-contributory. The patient had four siblings, all living and well.

The patient was seen by a surgical consultant who suggested splenectomy following a complete evaluation for congestive splenomegaly. Blood counts revealed a moderate anemia with hemoglobin of 10 grams; red blood cells, 3,000,000; and, a persistent leukopenia, averaging 2,400 white blood cells. Differential counts revealed granulocytes averaging 60 per cent, lymphocytes 40 per cent. Bleeding and coagulation times were normal. Urinalyses were essentially negative. Platelet counts averaged 120,000 per cubic millimeter. Red blood cell fragility tests were normal. The blood sedimentation rate was 48 millimeters per hour. The blood cholesterol was 200 milligrams per 100 ml. Icterus index was 25 units and the van den Bergh test was positive in the immediate direct phase. Quantitative serum bilirubin was 2 milligrams per 100 ml. The serologic test for syphilis was negative. The urine was strongly positive for bilirubin, and the urine urobilinogen was slightly elevated. Total serum proteins averaged 6 grams per 100 ml. and the A/G ratio was normal. The prothrombin activity was 100 per cent of normal and the heterophile agglutination tests were negative. The cephalin flocculation test was 4 plus in 48 hours. Bone marrow aspiration revealed normal marrow. Post-operatively, the icterus index rose to 60 units and the serum bilirubin to 4.5 milligrams per 100 ml. The cephalin flocculation test at this time was negative. The total proteins and A/G ratio remained the same. Twelve days following surgery, the patient was discharged to the care of his parents.

During the 2 year interval between the patient's discharge from the

hospital following splenectomy and his final admission and death, his course and activities were essentially normal. Two weeks prior to his final admission he had fever, cough, and chills. This did not respond to the usual household measures. On the night before admission he became delirious and irrational. There was a marked rise in temperature and his chills were severe. He was taken to his physician and at that time the temperature was 105 degrees. Alcohol sponge baths and hospitalization were advised. On the morning of admission the patient became nauseated and vomited. He passed numerous loose, clay-colored stools. The delirium continued, and the patient was rushed to the hospital.

Physical examination on admission revealed a moribund, cyanotic, icteric white male child. His respirations were 60 per minute, and auscultation of the chest revealed numerous bubbling ronchi and coarse moist rales. The liver was nodular and was palpated 6 centimeters below the right costal margin. The patient's delirium continued, and he died 2 hours after admission.

DISCUSSION

Dr. Roland B. Scott:

The history and the available physical and laboratory data in the protocol indicate that this child had a syndrome involving chiefly the liver and spleen. There was a history of neonatal jaundice; however, I think that we can exclude erythroblastosis fetalis because icterus was not noted until ten days of life and the family history is described as being non-contributory. There were four siblings, all living and well. There is nothing in the protocol to suggest the presence of other causes of neonatal jaundice, such as sepsis or infection of the umbilical cord, congenital syphilis, toxoplasmosis or cytomegalic inclusion disease. The non-contributory family history, the normal red cell fragility, and the absence of hemolytic crises and the normal bone marrow findings, I think, would exclude congenital hemolytic anemia. No mention is made of any significant x-ray findings. I presume that x-ray studies of the skeleton and esophagus were made. The enlargement of the liver and the spleen, together with the moderate anemia, thrombocytopenia, leukopenia and the markedly enlarged abdomen are consistent with hypersplenism and congestive splenomegaly probably of the secondary type. The bone marrow and other hematologic studies appear to rule our such blood dyscrasias as leukemia and primary anemias. There is nothing in the protocol to suggest reticuloendotheliosis. Infectious mononucleosis, which may cause jaundice and may mimic many other diseases, has apparently been excluded.

We are, therefore, left with a vascular cause for the splenomegaly, which is presumably congestive in nature. Contrary to the original theory of

Banti, congestive splenomegaly is now regarded as being secondary to factors which obstruct the splenic venous system. The primary disturbances may be located in the liver, in the extrahepatic portal vessels or in the splenic vein.

In the case under discussion, I believe that we must look to the liver itself for the primary source of the trouble. The child obviously had a cirrhotic liver on the basis of the clinical findings. In reporting on 40 cases of cirrhosis of the liver in children, Keller and Nute[1] classified cirrhosis of the liver in children etiologically as follows: 1. Obstructive biliary cirrhosis; 2. nodular or so-called portal cirrhosis; 3. post-necrotic cirrhosis (secondary to such toxic substances as carbon tetrachloride and chloroform); 4. congestive or cardiac type of cirrhosis; 5. erythroblastosis fetalis; 6. hepatolenticular degeneration of Wilson; and 7. unclassified cases.

Although the age of onset of jaundice at ten days of age is compatible with obstructive biliary cirrhosis, the survival of this patient for six years without ductal surgery practically excludes congenital atresia of the bile ducts. However, there is a report in the literature of a child who lived to be 9½ years old without the benefit of surgical relief. Moreover, the presence of urobilinogen in the urine is against the diagnosis of atresia of the bile ducts.

There was no history of ingestion or exposure of the child to hepatotoxic chemicals and drugs. Cardiac cirrhosis is excluded by the finding of a normal heart. Hepato-lenticular degeneration of Wilson usually begins in later childhood or during adult life and has characteristic ophthalmologic and neurological findings which are absent in this case. We are, therefore, left with what might be called diffuse nodular portal cirrhosis. Eleven of the 40 cases described by Keller and Nute and 7 of the 20 cases of cirrhosis in children described by Harrell and McBride[2] were portal in type.

The history and the findings, and also the laboratory data, particularly the liver function tests, are all compatible with portal cirrhosis and secondary congestive splenomegaly with hypersplenism. Although this case did not have abdominal ascites clinically, we are told that there was a large and very prominent abdomen and that the superficial veins were also prominent. There was an umbilical hernia. Ascites is often present in this syndrome, but it may be absent. As to the primary etiology, I would like to speculate a bit and suggest that this child may have had a prenatal hepatitis caused by passage of a virus across the placenta from the mother who was probably a healthy carrier. Stokes and others have described neonatal hepatitis and cirrhosis presumably due to the type B or SH virus. In some instances, this type of viral hepatitis may simulate congenital atresia of the bile ducts. It has been postulated that the SH virus may actually cause congenital anomalies in the biliary passages of the developing

fetus in a manner analogous to the rubella virus. Death in this patient was probably due to a complicating infection.

Needle biopsy of the liver[3] for microscopic examination and injection of the spleen with a contrast medium[4] for radiographic delineation of the portal venous system represent two techniques which have been described for differentiation between intrahepatic and extrahepatic obstructive factors in portal hypertension. These procedures were not done in this case; however the results obtained from liver function tests suggest intrahepatic disease.

The splenectomy performed in this case may have temporarily delayed the appearance of esophageal or gastrointestinal hemorrhages. At present, the recommended surgical procedure in infants and small children appears to be splenectomy and a splenorenal anastomosis[5]. In the case of intrahepatic obstruction (Hepatic cirrhosis), it may be advisable later to perform a portacaval shunt when the child is older. Primary splenectomy alone is no longer recommended because this procedure cannot permanently relieve portal hypertension and also by sacrificing the splenic vein, it excludes the possibility of performing a splenorenal anastomosis later.

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Dr. Grace H. Guin:

The findings at autopsy were as follows:

Some portions of the esophagus did show dilatation of the veins but no actual hemorrhage. Possibly if the child had lived longer hemorrhage might have taken place. The lungs showed pulmonary edema with some increase in mononuclear cells in the alveolar walls. The spleen was surgically absent. The liver showed an increase of about 40 per cent above the normal weight. The surface was nodular and yellowish-brown. On section at autopsy as at operation there was nodular cirrhosis. The lobules were distorted by connecting bands of fibrous tissue which pinched the hepatic cords off from one another, and the circulation instead of going through its usual channels was forced in abnormal directions. The fact that giant cells were not found does not mean that the child could not have had infectious hepatitis in the beginning. The fact that the process was active is shown by the presence of acute inflammatory cells. There was also an acute pericarditis. These findings suggest those seen in an acute overwhelming infection. Some areas of the liver were involved more than others.

Final Pathological Diagnosis:

1. Cirrhosis secondary to neonatal hepatitis
2. Interstitial pneumonia
3. Septicemia

Dr. Grace Guin:

After the surgical removal of the spleen, one may reason in this case, that the presence of infection provoked the reactive lymphoid follicles. In this case we have reason to believe that the child did have neonatal hepatitis with subsequent portal cirrhosis. Other workers believe that the cirrhosis which follows neonatal hepatitis is of the portal type. The Boston group feel that biliary cirrhosis is the end result. I would like to ask Dr. Scott what his experience with cases similar to this has been at Howard University.

Dr. Scott: I really do not know, Dr. Guin, but I imagine that the cirrhosis could be either portal or biliary.

Dr. E. Clarence Rice:

It is interesting to follow the evolution of our thinking in relation to the etiology of hepatic pathology. As we are able to influence disease by improved therapy we will continue to see changes which we rarely or possibly never witnessed before. Possibly the baby who is treated for erythroblastosis fetalis with present day methods may later show some hepatic changes which were not seen previously; or the child with cystic fibrosis of the pancreas whose life span is lengthened because of our ability to recognize and treat this condition early, may allow the development of a cardiac type of cirrhosis. Another example is the leukemic child who has been treated with the antifols, antipurines or steroids. Here the sudden dispersal or destruction of the leukemic cells which densely infiltrated the liver may result in a rapid and uneven shrinkage of the organ, the vacant areas formerly occupied by the neoplastic cells eventually being replaced by connective tissue. I am sure that in the future we shall see other changes due to other etiological factors because of increasingly effective forms of treatment.

One may raise the question of the possible effects of removal of the spleen on rendering the young patient more susceptible to infection. We have seen evidence that the splenectomized child is more likely to become a victim of fulminating infections than one who has not undergone this type of surgery. Reports in the literature indicate that the increased susceptibility of the infant and young child to septicemia and meningitis is sufficiently great as to make one consider this possible consequence before coming to the decision to remove the spleen of a young child.

Children with liver disease may have an increased likelihood of infection

by *Hemophilus influenzae*, two of our patients having died of this type of infection. These findings may be only coincidental however.

Dr. Neville K. Connolly:

In discussing a splenectomy in these cases, I think we have to remember that all surgery except that which is purely reconstructive is a confession of medical failure. Whenever one operates on an infant or child where the diagnosis is not absolutely certain, one must do so with all the possibilities that one may find in one's mind. One must not have a preconceived conviction that he is going to do a certain procedure no matter what he finds, and one must be prepared for all the types of surgery that might be necessary for any of the conditions that could cause the picture. In cases such as this one must be cautious about splenectomy because if there is portal hypertension a shunt may be necessary, and in many cases a lienorenal shunt would be the operation of choice provided a splenectomy had not been done beforehand. One should, however, be prepared to estimate the degree of portal hypertension, and also with the aid of radio-opaque dyes to be sure that there is no block in the portal or splenic vein. In some cases a portacaval shunt is the only one that would have a chance, but even this is chiefly of benefit only when there is evidence of esophageal bleeding.

Dr. F. R. Leyva:

I would like to ask Dr. Guin if there was any evidence of regenerative nodule formation besides the postnecrotic scarring and active inflammatory reaction of the liver parenchyma. As to the cause of the portal cirrhosis, I understand it is frequently impossible to decide when an episode of jaundice represents an attack of viral hepatitis or is the first sign of liver failure. In a study of 98 patients with cirrhosis of the liver by Craig, Gellis, and Hsia,[1] 30 cases were associated with hepatitis and of these only 5 were actually associated with viral hepatitis. In contrast, many cases were associated with neonatal hepatitis but not necessarily viral in origin. The same authors stated that cirrhosis of the liver is a rare complication of viral hepatitis, concluding that in their experience with 200 cases of proven hepatitis followed for four years, none has developed chronic hepatitis or cirrhosis.

Dr. Guin:

No evidence of regenerative nodule formation was noted.

Dr. Leyva:

Recent studies have demonstrated that other factors besides contracting scar tissue produce obstruction of the portal vein. It seems likely that the pressure from regenerating hepatic artery transmitted to the portal system

through large anastomotic channels are added factors in the development of portal hypertension.

The differential diagnosis between primary or secondary portal hypertension is important from the viewpoint of treatment. Venous shunts are particularly indicated in the primary type. The following points suggest primary portal hypertension: a) history of bacterial infection during infancy; b) no evidence of jaundice or other signs of liver damage prior to the onset of symptoms; c) splenomegaly and hematemesis as presenting symptoms; d) normal liver function test.

In secondary types of portal hypertension there is a previous history of jaundice or liver enlargement and tenderness; ascites usually occurs before splenomegaly or hematemesis, and above all, positive liver function tests occur. On occasion it is impossible to differentiate some cases clinically and the type of portal hypertension can only be determined by liver biopsy.

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